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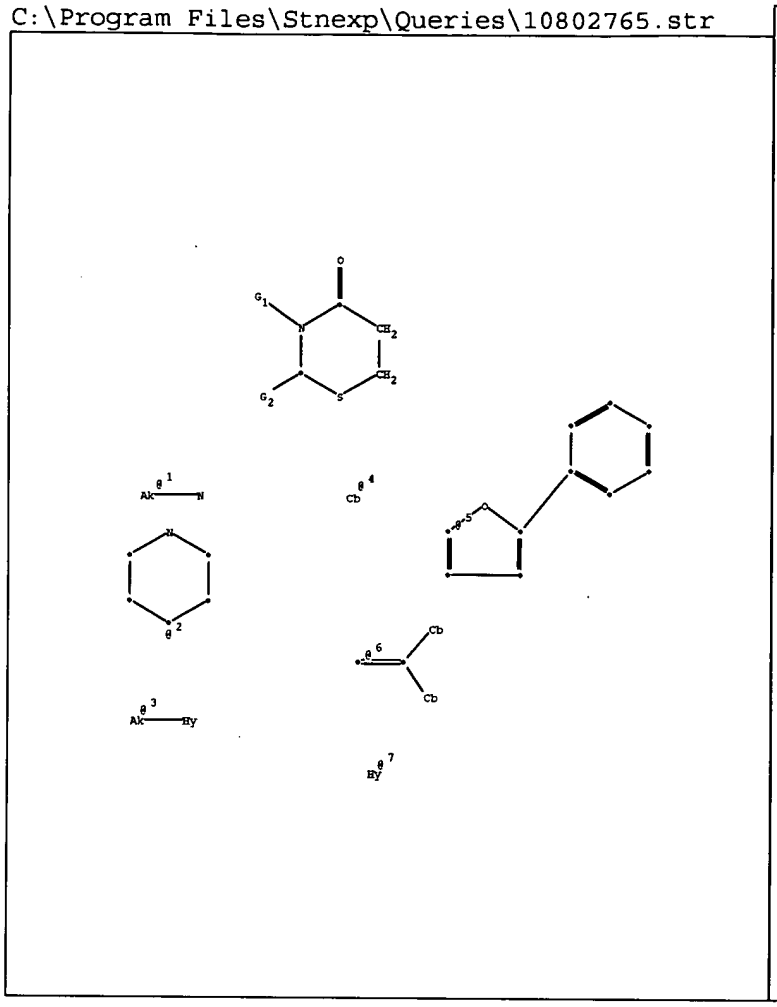

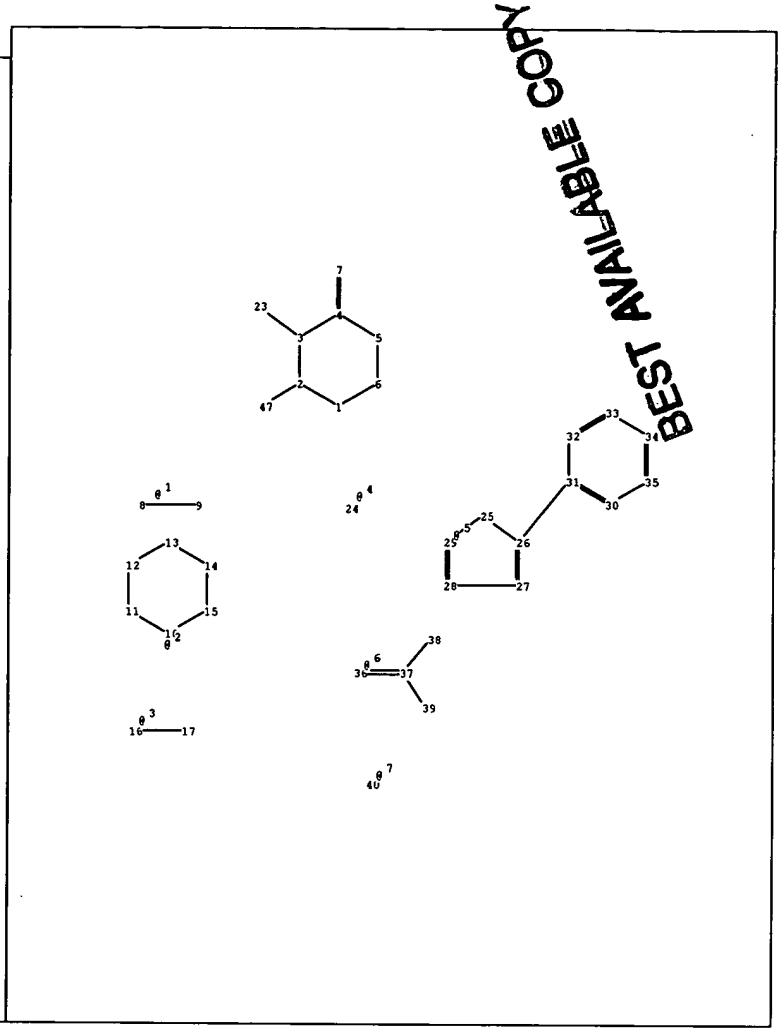

chain nodes :
7 8 16 17 23 24 36 37 38 39 40 47
ring nodes :
1 2 3 4 5 6 10 11 12 13 14 15 25 26 27 28 29 30 31 32 33 34 35
ring/chain nodes :
9
chain bonds :
2-47 3-23 4-7 8-9 16-17 26-31 36-37 37-38 37-39
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 25-26 25-29
26-27 27-28 28-29 30-31 30-35 31-32 32-33 33-34 34-35
exact/norm bonds :
1-2 1-6 2-3 2-47 3-4 3-23 4-5 4-7 5-6 8-9 10-11 10-15 11-12 12-13 13-14
14-15 16-17 25-26 25-29 26-27 27-28 28-29
exact bonds :
26-31 36-37 37-38 37-39
normalized bonds :
30-31 30-35 31-32 32-33 33-34 34-35

G1:[*1],[*2],[*3]

G2:[*4],[*5],[*6],[*7]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS 17:Atom 23:CLASS 24:Atom
25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 33:Atom 34:Atom
35:Atom 36:CLASS 37:CLASS 38:Atom 39:Atom 40:Atom 47:CLASS
Generic attributes :
17:

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=> d his

     (FILE 'HOME' ENTERED AT 12:07:18 ON 14 APR 2005)

     FILE 'REGISTRY' ENTERED AT 12:07:30 ON 14 APR 2005
L1                STRUCTURE UPLOADED
L2              0 S L1
L3              8 S L1 FULL

     FILE 'CAPLUS' ENTERED AT 12:08:11 ON 14 APR 2005
L4             15 S L3

=> d que l4 stat
L1                STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L3              8 SEA FILE=REGISTRY SSS FUL L1
L4             15 SEA FILE=CAPLUS ABB=ON  PLU=ON  L3


=> d 1-15 bib abs hitstr
```

L4 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:76766 CAPLUS
DN 138:131144
TI Aryl-substituted thiazolidinones and therapeutic use thereof
IN Sun, Qun; Kyle, Donald J.
PA Euro-Celtique, S.A., Luxembourg
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

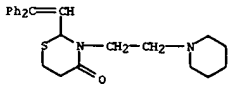
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003008398	A1	20030130	WO 2002-US22367	20020716
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003109521	A1	20030612	US 2002-195530	20020716
	EP 1417187	A1	20040512	EP 2002-763275	20020716
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	JP 2004538285	T2	20041224	JP 2003-513957	20020716
	US 2004176364	A1	20040909	US 2004-802765	20040318
PRAI	US 2001-305099P	P	20010716		
	US 2002-195530	A3	20020716		
	WO 2002-US22367	W	20020716		

OS MARPAT 138:131144
GI

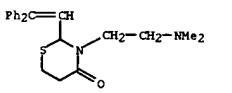
I

AB The invention discloses aryl-substituted thiazolidinones I [n = 1, 2; R1 = YN(R3)(R4) (Y = alkylene; R3, R4 = H, alkyl, aryl, or R3 and R4 together form alkylene chain having 4-5 C optionally interrupted by N or O), pyridylalkyl, optionally substituted piperidin-4-yl; R2 = optionally substituted phenoxyphenyl, optionally substituted phenylthiophenyl, optionally substituted benzyloxyphenyl, etc.], or a pharmaceutically acceptable salt or solvate thereof. The invention also discloses the use of I for the treatment of neuronal damage following global and focal ischemia, for the treatment or prevention of neurodegenerative conditions, e.g. amyotrophic lateral sclerosis, and for the treatment, prevention or

L4 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
amelioration of both acute and chronic pain, of depression, as local anesthetics, as antiarrhythmics and for the treatment or prevention of diabetic neuropathy. The compds. of the invention are sodium channel blockers.
IT 491864-53-0 491864-87-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aryl-substituted thiazolidinones and therapeutic use)
RN 491864-53-0 CAPLUS
CN 4H-1,3-Thiazin-4-one, 2-(2,2-diphenylethenyl)tetrahydro-3-[2-(1-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

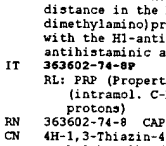


RN 491864-87-0 CAPLUS
CN 4H-1,3-Thiazin-4-one, 3-[2-(dimethylamino)ethyl]-2-(2,2-diphenylethenyl)tetrahydro- (9CI) (CA INDEX NAME)



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:428220 CAPLUS
DN 135:272658
TI Intramolecular C-H--O interaction between lactam oxygen and N-alkyl protons
AU Barone, V.; Bolognese, A.; Correale, G.; Diurno, M. V.; Gomez-Monterrey, I.; Mazzoni, O.
CS Dipartimento di Chimica, Universita di Napoli "Federico II", Naples, Italy
SO Journal of Molecular Graphics & Modelling (2001), 19(3/4), 318-324
CODEN: JMGMFI; ISSN: 1093-3263
PB Elsevier Science Inc.
DT Journal
LA English
AB We report evidence of an unusual C-H--O interaction between an α-methylene hydrogen of the alkylamine chain of substituted (N,N-dimethylamino)propyl-azetidinones, substituted (N,N-dimethylamino)propyl-thiazolidinones and substituted (N,N-dimethylamino)propyl-thiazinone and the lactam carbonyl oxygen. NMR anal. results, supported by mol. mechanics predictions, were in agreement with ab initio calcns. The observed interaction shortening the nitrogen-nitrogen distance in the H1-histamine antagonist, 2-(4-methylphenyl)-3-[3-(N,N-dimethylamino)propyl]-1,3-thiazolidin-4-one, could explain its fitting with the H1-antihistaminic pharmacophoric model and the high antihistaminic activity.
IT 363602-74-8P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(intramol. C-H--O interaction between lactam oxygen and N-alkyl protons)
RN 363602-74-8 CAPLUS
CN 4H-1,3-Thiazin-4-one, 3-[3-(dimethylamino)propyl]tetrahydro-2-(4-methylphenyl)- (9CI) (CA INDEX NAME)



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:819473 CAPLUS
DN 134:5159
TI Preparation of tripeptoid analogs as serine protease inhibitors
IN Gyorkos, Albert C.; Spruce, Lyle W.
PA Cortech, Inc., USA
SO U.S., 107 pp., Cont-in-part of U. S. Ser. No. 761,190.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 18

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6150334	A	20001121	US 1997-985201	19971204
	US 5618792	A	19970408	US 1994-345820	19941121
	US 5807829	A	19980915	US 1996-761190	19961206
	CA 2272548	AA	19980611	CA 1997-2272548	19971205
	WO 9824806	A2	19980611	WO 1997-US21636	19971205
	WO 9824806	A3	19981015		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9855894	A1	19980629	AU 1998-55894	19971205
	AU 734615	B2	20010621		
	EP 954526	A2	19991110	EP 1997-952232	19971205
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	CN 1247542	A	20000315	CN 1997-180392	19971205
	TR 9901681	T2	20000321	TR 1999-9901681	19971205
	JP 2001507679	T2	20010612	JP 1998-525656	19971205
	JP 3220169	B2	20011022		
	JP 2001192398	A2	20010717	JP 2000-197432	19971205
	TR 200103270	T2	20030321	TR 2001-200103270	19971205
	RU 2217436	C2	20031127	RU 1999-114606	19971205
	US 6037325	A	20000314	US 1998-69823	19980430
	US 6001813	A	19991214	US 1998-90046	19980603
	NO 9902734	A	19990802	NO 1999-2734	19990604
	MX 9905240	A	20000531	MX 1999-5240	19990604
PRAI	US 1994-345820	A2	19941121		
	US 1996-761190	A2	19961206		
	US 1996-698575	A1	19960815		
	US 1996-760916	A	19961206		
	US 1996-761313	A	19961206		
	US 1996-762381	A	19961206		
	US 1996-771317	A	19961206		
	US 1997-984881	A	19971204		
	US 1997-984884	A	19971204		
	US 1997-985056	A	19971204		
	US 1997-985201	A	19971204		
	US 1997-985298	A	19971204		
	JP 1998-525656	A3	19971205		
	WO 1997-US21636	W	19971205		

OS MARPAT 134:5159
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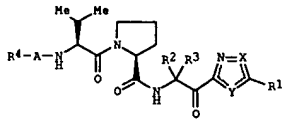
L4 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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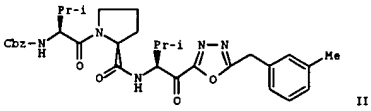


II

AB Tripeptides I [X, Y = O, N, or S, provided that at least one of X or Y = N; R1 = (un)substituted (C5-12)aryl, (C5-12)arylalkyl, (C5-12)arylalkenyl, fused (C5-12)aryl-cycloalkyl, alkyl- or alkenyl-fused (C5-12)aryl-cycloalkyl optionally comprising one or more heteroatoms selected from N, S, or non-peroxide O; R2, R3 = H or alkyl; A = CO, NHCO, SO2, O2C, or CH2; R4 = H, alkyl, alkenyl, cycloalkyl, aryl, or arylalkyl (with provisos)] were prepared as serine protease inhibitors, including inhibitors of human neutrophil elastase. Thus, peptide I (Cbz = benzyloxycarbonyl) (CE-2072) was prepared and showed Ki = 0.025 nM for inhibition of elastase.

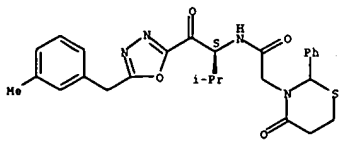
IT **208845-59-4P**, Ce-2118
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tripeptoid analogs as serine protease inhibitors)

RN 208845-59-4 CAPLUS

CN 2H-1,3-Thiazine-3(4H)-acetamide, dihydro-N-[(1S)-2-methyl-1-[[5-[(3-methylphenyl)methyl]-1,3,4-oxadiazol-2-yl]carbonyl]propyl]-4-oxo-2-phenyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:47017 CAPLUS

DN 132:78559

TI Preparation of heterocyclic compounds as serine protease inhibitors

IN Gyorkos, Albert; Spruce, Lyle W.

PA Cortech Inc., USA

SO U.S., 107 pp., Cont.-in-part of U.S. 5,891,852.
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 18

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6015791	A	20000118	US 1997-984881	19971204
	US 5618792	A	19970408	US 1994-345820	19941121
	US 5891852	A	19990406	US 1996-762381	19961206
	CA 2272548	AA	19980611	CA 1997-2272548	19971205
	WO 9824806	A2	19980611	WO 1997-US21636	19971205
	WO 9824806	A3	19981015		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9855894	A1	19980629	AU 1998-55894	19971205
	AU 734615	B2	20010621		
	EP 954526	A2	19991110	EP 1997-952232	19971205
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CN 1247542	A	20000315	CN 1997-180392	19971205
	TR 9901681	T2	20000321	TR 1999-9901681	19971205
	JP 2001507679	T2	20010612	JP 1998-525656	19971205
	JP 3220169	B2	20011022		
	JP 2001192398	A2	20010717	JP 2000-197432	19971205
	TR 200103270	T2	20030321	TR 2001-200103270	19971205
	RU 2217436	C2	20031127	RU 1999-114606	19971205
	US 6037325	A	20000314	US 1998-69823	19980430
	NO 9902734	A	19990802	NO 1999-2734	19990604
	MX 9905240	A	20000531	MX 1999-5240	19990604
PRAI	US 1994-345820	A2	19941121		
	US 1996-762381	A2	19961206		
	US 1996-698575	A1	19960815		
	US 1996-760916	A	19961206		
	US 1996-761190	A	19961206		
	US 1996-761313	A	19961206		
	US 1996-771317	A	19961206		
	US 1997-984881	A	19971204		
	US 1997-984884	A	19971204		
	US 1997-985056	A	19971204		
	US 1997-985201	A	19971204		
	US 1997-985298	A	19971204		
	JP 1998-525656	A3	19971205		
	WO 1997-US21636	W	19971205		

OS MARPAT 132:78559

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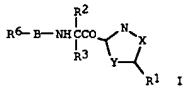
L4 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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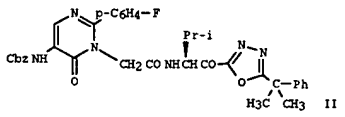


II

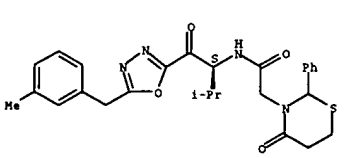
AB The present invention relates to a series of compds. of general structure I [X, Y = O, N, or S provided that at least one of X or Y = N; R1 = C5-12 aryl, C5-12 arylalkyl, or C5-12 arylalkenyl with at least one N, S, and O; R2, R3 = H or alkyl; B = S(O)2 or C(O); R6 = heterocycles (generic structures given)] that are useful as serine protease inhibitors, including inhibitors for human neutrophil elastase. In an in vitro test for inhibition of elastase, the title compound II shows the Ki value of 78.3. Compds. of the invention are useful in treating conditions such as adult respiratory distress syndrome, septic shock, and multiple organ failure.

IT **208845-59-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic compds. as serine protease inhibitors)

RN 208845-59-4 CAPLUS

CN 2H-1,3-Thiazine-3(4H)-acetamide, dihydro-N-[(1S)-2-methyl-1-[[5-[(3-methylphenyl)methyl]-1,3,4-oxadiazol-2-yl]carbonyl]propyl]-4-oxo-2-phenyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:794318 CAPLUS
DN 132:23197
TI Preparation of N-substituted prolinyl peptide analogs as serine protease inhibitors
IN Gyorkos, Albert; Spruce, Lyle W.
PA Cortech Inc., USA
SO U.S., 107 pp., Cont.-in-part of U.S. 5,869,455.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 18

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6001811	A	19991214	US 1997-984884	19971204
	US 5618792	A	19970408	US 1994-345820	19941121
	US 5869455	A	19990209	US 1996-761313	19961206
	CA 2272548	AA	19980611	CA 1997-2272548	19971205
	WO 9824806	A2	19980611	WO 1997-US21636	19971205
	WO 9824806	A3	19981015		
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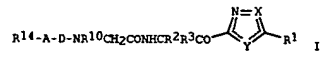
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9855894	A1	19980629	AU 1998-55894	19971205
	AU 734615	B2	20010621		
	EP 954526	A2	19991110	EP 1997-952232	19971205
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CN 1247542	A	20000315	CN 1997-180392	19971205
	TR 9901681	T2	20000321	TR 1999-9901681	19971205
	JP 2001507679	T2	20010612	JP 1998-525656	19971205
	JP 3220169	B2	20011022		
	TR 200103270	T2	20030321	TR 2001-200103270	19971205
	RU 2217436	C2	20031127	RU 1999-114606	19971205
	US 6037325	A	20000314	US 1998-69823	19980430
	NO 9902734	A	19990802	NO 1999-2734	19990604
	MX 9905240	A	20000531	MX 1999-5240	19990604
PRAI	US 1994-345820	A2	19941121		
	US 1996-761313	A2	19961206		
	US 1996-698575	A1	19960815		
	US 1996-760916	A	19961206		
	US 1996-761190	A	19961206		
	US 1996-762381	A	19961206		
	US 1996-771317	A	19961206		
	US 1997-984881	A	19971204		
	US 1997-984884	A	19971204		
	US 1997-985056	A	19971204		
	US 1997-985201	A	19971204		
	US 1997-985298	A	19971204		
	WO 1997-US21636	W	19971205		

OS MARPAT 132:23197
GI

L4 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



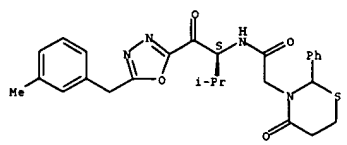
I

AB Proline analogs I [X, Y = O, S, N or substituted N; R1 = (un)substituted alkyl, alkenyl, or alkynyl, hydroxy, amino, alkylamino, dialkylamino, cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, cycloalkenyl, alkylcycloalkenyl, alkenylcycloalkenyl, aryl, arylalkyl, arylalkenyl, etc.; R2, R3 = H, (un)substituted alkyl or alkenyl, -RCOR', -RCO2R', -RNR'R''RO, or -RCONR'R'', where R is alkyl or alkenyl and R', R'', and RO are H, alkyl, alkenyl, cycloalkyl, aryl, cycloalkyl, etc.; R10 = aryl, arylalkyl, arylalkenyl, cycloalkyl, alkylcycloalkyl, etc.; D is a direct bond or an amino acid selected from proline, isoleucine, cyclohexylalanine, or cysteine optionally substituted at sulfur, A is a direct bond, CO, NHCO, SO2, OCO, CH2; R14 = H, alkyl, alkenyl, aryl, arylalkyl, cycloalkyl, alkylcycloalkyl, etc.] were prepared as serine protease inhibitors. Thus, (benzyloxycarbonyl)-L-valyl-N-[1(S)-[[5-(3-methylbenzyl)-1,3,5-oxadiazolyl]carbonyl]-2-methylpropyl]-L-prolinamide was prepared and showed Ki = 0.025 nM for inhibition of human neutrophil elastase.

IT **208845-59-4P**, CE 2118
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prolinyl peptide analogs as serine protease inhibitors)

RN 208845-59-4 CAPLUS
CN 2H-1,3-Thiazine-3(4H)-acetamide, dihydro-N-[(1S)-2-methyl-1-[[5-[(3-methylphenyl)methyl]-1,3,4-oxadiazol-2-yl]carbonyl]propyl]-4-oxo-2-phenyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:779215 CAPLUS
DN 132:36032
TI Preparation of prolinyl peptide analogs as serine protease inhibitors
IN Gyorkos, Albert; Spruce, Lyle W.
PA Cortech Inc., USA
SO U.S., 110 pp., Cont.-in-part of U.S. 5,801,148.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 18

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5998379	A	19991207	US 1997-985056	19971204
	US 5618792	A	19970408	US 1994-345820	19941121
	US 5801148	A	19980901	US 1996-771317	19961206
	CA 2272548	AA	19980611	CA 1997-2272548	19971205
	WO 9824806	A2	19980611	WO 1997-US21636	19971205
	WO 9824806	A3	19981015		
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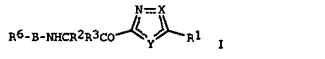
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9855894	A1	19980629	AU 1998-55894	19971205
	AU 734615	B2	20010621		
	EP 954526	A2	19991110	EP 1997-952232	19971205
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CN 1247542	A	20000315	CN 1997-180392	19971205
	TR 9901681	T2	20000321	TR 1999-9901681	19971205
	JP 2001507679	T2	20010612	JP 1998-525656	19971205
	JP 3220169	B2	20011022		
	TR 200103270	T2	20030321	TR 2001-200103270	19971205
	RU 2217436	C2	20031127	RU 1999-114606	19971205
	US 6037325	A	20000314	US 1998-69823	19980430
	US 6100238	A	20000808	US 1998-89587	19980603
	NO 9902734	A	19990802	NO 1999-2734	19990604
	MX 9905240	A	20000531	MX 1999-5240	19990604
PRAI	US 1994-345820	A2	19941121		
	US 1996-771317	A2	19961206		
	US 1996-698575	A1	19960815		
	US 1996-760916	A	19961206		
	US 1996-761190	A	19961206		
	US 1996-761313	A	19961206		
	US 1996-762381	A	19961206		
	US 1997-984881	A	19971204		
	US 1997-984884	A	19971204		
	US 1997-985056	A	19971204		
	US 1997-985201	A	19971204		
	US 1997-985298	A	19971204		
	WO 1997-US21636	W	19971205		

OS MARPAT 132:36032
GI

L4 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



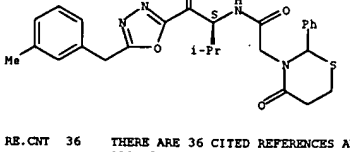
I

AB Proline analogs I [X, Y = O, S, N or substituted N; R1 = (un)substituted alkyl, alkenyl, or alkynyl, hydroxy, amino, alkylamino, dialkylamino, cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, cycloalkenyl, alkylcycloalkenyl, alkenylcycloalkenyl, aryl, arylalkyl, arylalkenyl, etc.; R2, R3 = H, (un)substituted alkyl or alkenyl, -RCOR', -RCO2R', -RNR'R''RO, or -RCONR'R'', where R is alkyl or alkenyl and R', R'', and RO are H, alkyl, alkenyl, cycloalkyl, aryl, cycloalkyl, etc.; B = SO2, CO, OCO, CH2CO; R6 = aryl, arylalkyl, cycloalkyl, alkylcycloalkyl, or R14-A-D-NR7CHR8-, where R7R8 is o-(CH2)nC6H4(CH2)m (m, n = 0, 1), D is a direct bond or an amino acid selected from proline, isoleucine, cyclohexylalanine, or cysteine optionally substituted at sulfur, A is a direct bond, CO, NHCO, SO2, OCO, CH2; R14 = H, alkyl, alkenyl, aryl, arylalkyl, cycloalkyl, alkylcycloalkyl, etc.] were prepared as serine protease inhibitors. Thus, (benzyloxycarbonyl)-L-valyl-N-[1(S)-[[5-(3-methylbenzyl)-1,3,5-oxadiazolyl]carbonyl]-2-methylpropyl]-L-prolinamide was prepared and showed Ki = 0.025 nM for inhibition of human neutrophil elastase.

IT **208845-59-4P**, CE 2118
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prolinyl peptide analogs as serine protease inhibitors)

RN 208845-59-4 CAPLUS
CN 2H-1,3-Thiazine-3(4H)-acetamide, dihydro-N-[(1S)-2-methyl-1-[[5-[(3-methylphenyl)methyl]-1,3,4-oxadiazol-2-yl]carbonyl]propyl]-4-oxo-2-phenyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:231191 CAPLUS
DN 130:252684
TI Preparation of fused cycloheptane azole heterocyclic peptoids as serine protease inhibitors
IN Gyorkos, Albert; Spruce, Lyle W.
PA Cortech, Inc., USA
SO U.S., 61 pp., Cont.-in-part of U.S. 5,618,792.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 18

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5891852	A	19990406	US 1996-762381	19961206
	US 5618792	A	19970408	US 1994-345820	19941121
	CA 2205198	AA	19960530	CA 1995-2205198	19951117
	CA 2205198	C	20020604		
	CN 1170414	A	19980114	CN 1995-196952	19951117
	ES 2145936	T3	20000716	ES 1995-940031	19951117
	PT 793674	T	20001130	PT 1995-940031	19951117
	ZA 9509819	A	19960530	ZA 1995-9819	19951120
	TW 474924	B	20020201	TW 1995-84112388	19951120
	IL 116078	A1	19991231	IL 1995-116078	19951121
	US 5874585	A	19990223	US 1996-698575	19960815
	US 6015791	A	20000118	US 1997-984881	19971204
	CA 2272548	AA	19980611	CA 1997-2272548	19971205
	WO 9824806	A2	19980611	WO 1997-US21636	19971205
	WO 9824806	A3	19981015		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9855894	A1	19980629	AU 1998-55894	19971205
	AU 734615	B2	20010621		
	EP 954526	A2	19991110	EP 1997-952232	19971205
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CN 1247542	A	20000315	CN 1997-180392	19971205
	TR 9901681	T2	20000321	TR 1999-9901681	19971205
	BR 9713684	A	20000328	BR 1997-13684	19971205
	JP 2001507679	T2	20010612	JP 1998-525656	19971205
	JP 3220169	B2	20011022		
	JP 2001192398	A2	20010717	JP 2000-197432	19971205
	TR 200103270	T2	20030321	TR 2001-200103270	19971205
	RU 2217436	C2	20031127	RU 1999-114606	19971205
	TW 593340	B	20040621	TW 1997-86118340	19971205
	US 6037325	A	20000314	US 1998-69823	19980430
	NO 9902734	A	19990802	NO 1999-2734	19990604
	MX 9905240	A	20000531	MX 1999-5240	19990604
PRAI	US 1994-345820	A2	19941121		
	US 1996-698575	A1	19960815		
	US 1996-760916	A	19961206		

L4 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

	US 1996-761190	A	19961206		
	US 1996-761313	A	19961206		
	US 1996-762381	A2	19961206		
	US 1996-771317	A	19961206		
	US 1997-984881	A	19971204		
	US 1997-984884	A	19971204		
	US 1997-985056	A	19971204		
	US 1997-985201	A	19971204		
	US 1997-985298	A	19971204		
	JP 1998-525656	A3	19971205		
	WO 1997-US21636	W	19971205		

GI

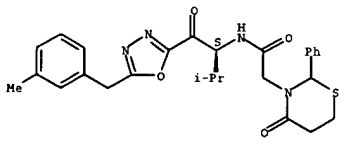
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to certain substituted oxadiazole, thiadiazole and triazole peptoids I [X, Y = O, N, S; at least one of X or Y = N; R1 = alkyl, alkenyl (un)substituted with halo or OH; alkynyl, alkyl-CO2Me, dialkylamino, alkyldialkylamino; cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, C5-12 aryl, C5-12 arylalkyl, C5-12 arylalkenyl optionally containing ≥1 N, S, O atoms, and optionally substituted; R2, R3, R21, R31 = independently H, alkyl, alkylthio, alkylthioalkyl, cycloalkyl, alkylcycloalkyl, Ph, phenylalkyl optionally substituted with guanidine, carboalkoxy, OH, haloalkyl, alkylthio, alkylguanidine, dialkylguanidine, amidine; B = SO2, CO; R6 = fused cycloheptane ring system Q1-Q3; R13, R15 = independently H, alkyl, halo, alkoxy, carboalkoxy, cycloalkoxy, carboxyl, alkylthio, amino, alkylamino or dialkylamino; aryl, fused aryl, cycloalkyl optionally containing ≥1 O, N, S atoms, and optionally substituted with halo or alkyl; R14 = H, aminoalkyl, alkenyl; (un)substituted cycloalkyl, aryl, arylalkyl, fused aryl-cycloalkyl optionally containing ≥1 N, O, S atoms] and pharmaceutically acceptable salts thereof, which are useful as inhibitors of human neutrophil elastase (HNE) for the treatment of HNE-mediated processes implicated in conditions such as adult respiratory distress syndrome, septic shock and multiple organ failure. A series of studies also have indicated the involvement HNE in myocardial ischemia-reperfusion injury, emphysema. R14 = H, aminoalkyl, alkenyl; cycloalkyl, aryl, arylalkyl, fused aryl-cycloalkyl optionally containing ≥1 N, O, S atoms, and optionally substituted with alkyl, halo, alkoxy, amino, alkylamino, dialkylamino, carboxy, alkenyl, alkynyl, haloalkoxy, carboalkoxy, alkylcarboxamido, aryl, arylcarboxamido, alkylthio, haloalkylthio;. HNE-mediated processes are implicated in other conditions such as arthritis, periodontal disease, glomerulonephritis, dermatitis, psoriasis, cystic fibrosis, chronic bronchitis, atherosclerosis, Alzheimer's disease, organ transplantation, corneal ulcers, and invasion behavior of malignant tumors. Thus, coupling of hexahydroazepinoindolecarboxylic acid II (Fmoc = 9-fluorenylmethoxycarbonyl) with amino alc. III (preparation given), followed by Swern oxidation and deprotection gave desired title compound IV. IV inhibited human neutrophil elastase with Ki = 10.0 nM.

IT **208845-59-4P**

L4 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of fused cycloheptane azole heterocyclic peptoids as serine protease inhibitors)
RN 208845-59-4 CAPLUS
CN 2H-1,3-Thiazine-3(4H)-acetamide, dihydro-N-[(1S)-2-methyl-1-[[5-[(3-methylphenyl)methyl]-1,3,4-oxadiazol-2-yl]carbonyl]propyl]-4-oxo-2-phenyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:104503 CAPLUS
DN 130:125411
TI Preparation of N-substituted derivatives of azole heterocyclic peptoids as serine protease inhibitors
IN Gyorkos, Albert; Spruce, Lyle W.
PA Cortech, Inc., USA
SO U.S., 63 pp., Cont.-in-part of U.S. Ser. No. 345,820.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 18

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5869455	A	19990209	US 1996-761313	19961206
	US 5618792	A	19970408	US 1994-345820	19941121
	CA 2205198	AA	19960530	CA 1995-2205198	19951117
	CA 2205198	C	20020604		
	CN 1170414	A	19980114	CN 1995-196952	19951117
	ES 2145936	T3	20000716	ES 1995-940031	19951117
	PT 793674	T	20001130	PT 1995-940031	19951117
	ZA 9509819	A	19960530	ZA 1995-9819	19951120
	TW 474924	B	20020201	TW 1995-84112388	19951120
	IL 116078	A1	19991231	IL 1995-116078	19951121
	US 5874585	A	19990223	US 1996-698575	19960815
	US 6001811	A	19991214	US 1997-984884	19971204
	CA 2272548	AA	19980611	CA 1997-2272548	19971205
	WO 9824806	A2	19980611	WO 1997-US21636	19971205
	WO 9824806	A3	19981015		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9855894	A1	19980629	AU 1998-55894	19971205
	AU 734615	B2	20010621		
	EP 954526	A2	19991110	EP 1997-952232	19971205
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CN 1247542	A	20000315	CN 1997-180392	19971205
	TR 9901681	T2	20000321	TR 1999-9901681	19971205
	BR 9713684	A	20000328	BR 1997-13684	19971205
	JP 2001507679	T2	20010612	JP 1998-525656	19971205
	JP 3220169	B2	20011022		
	JP 2001192398	A2	20010717	JP 2000-197432	19971205
	TR 200103270	T2	20030321	TR 2001-200103270	19971205
	RU 2217436	C2	20031127	RU 1999-114606	19971205
	TW 593340	B	20040621	TW 1997-86118340	19971205
	US 6037325	A	20000314	US 1998-69823	19980430
	NO 9902734	A	19990802	NO 1999-2734	19990604
	MX 9905240	A	20000531	MX 1999-5240	19990604
PRAI	US 1994-345820	A2	19941121		
	US 1996-698575	A1	19960815		
	US 1996-760916	A	19961206		
	US 1996-761190	A	19961206		
	US 1996-761313	A2	19961206		
	US 1996-762381	A	19961206		
	US 1996-771317	A	19961206		

L4 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

	US 1997-984881	A	19971204
	US 1997-984884	A	19971204
	US 1997-985056	A	19971204
	US 1997-985201	A	19971204
	US 1997-985298	A	19971204
	JP 1998-525656	A3	19971205
	WO 1997-US21636	W	19971205

OS MARPAT 130:125411
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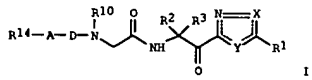
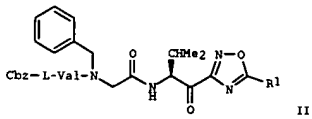


I



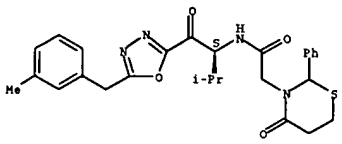
II

AB The present invention relates to certain substituted oxadiazole, thiadiazole and triazole peptoids I [X, Y = O, N, S; at least one of X or Y = N; R1 = alkyl or alkenyl optionally substituted with halo or hydroxy; alkynyl, alkyl-CO2Me, dialkylamino, alkyldialkylamino; or cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, C5-12 aryl, C5-12 arylalkyl, C5-12 arylalkenyl optionally containing 1 or more heteroatoms N, S, O, and optionally substituted; R2, R3 = independently H, alkyl, alkylthio, alkylthioalkyl, cycloalkyl, alkylcycloalkyl, Ph, phenylalkyl optionally substituted with guanidine, carboalkoxy, OH, haloalkyl, alkylthio, alkylguanidine, dialkylguanidine or amidine; R10 = C5-6 aryl, C5-6 arylalkyl, C5-6 arylalkenyl, cycloalkyl, arylcycloalkyl optionally containing
1 or more heteroatoms N, S, O, and optionally substituted; D = bond, CO, amino acid residue; A = bond, CO, NHCO, SO2, O2C, CH2; R14 = H, alkyl, alkenyl, cycloalkyl, aryl, arylalkyl, fused aryl-cycloalkyl optionally containing 1 or more heteroatoms N, O, S, and optionally substituted], and pharmaceutically acceptable salts thereof, which are useful as inhibitors of human neutrophil elastase (HNE) for the treatment of HNE-mediated processes implicated in conditions such as adult respiratory distress syndrome, septic shock and multiple organ failure. A series of studies also have indicated the involvement HNE in myocardial ischemia-reperfusion injury, emphysema. HNE-mediated processes are implicated in other conditions such as arthritis, periodontal disease, glomerulonephritis, dermatitis, psoriasis, cystic fibrosis, chronic bronchitis, atherosclerosis, Alzheimer's disease, organ transplantation, corneal

L4 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
ulcers, and invasion behavior of malignant tumors. Thus, oxadiazolyl tripeptoid II (R1 = CH2C6H4CF3-3; Cbz = PhCH2O2C) inhibited human neutrophil elastase with Ki = 0.98 nM.

IT **208845-59-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of azole heterocyclic peptoids as serine protease inhibitors)
RN 208845-59-4 CAPLUS
CN 2H-1,3-Thiazine-3(4H)-acetamide, dihydro-N-[(1S)-2-methyl-1-[[5-[(3-methylphenyl)methyl]-1,3,4-oxadiazol-2-yl]carbonyl]propyl]-4-oxo-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:56366 CAPLUS
DN 130:125406
TI Preparation of azole heterocyclic peptoids containing keto or diketo ring systems as serine protease inhibitors
IN Gyorkos, Albert; Spruce, Lyle W.
PA Cortech, Inc., USA
SO U.S., 67 pp., Cont.-in-part of U.S. 5,618,792.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 18

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5861380	A	19990119	US 1996-760916	19961206
	US 5618792	A	19970408	US 1994-345820	19941121
	CA 2205198	AA	19960530	CA 1995-2205198	19951117
	CA 2205198	C	20020604		
	CN 1170414	A	19980114	CN 1995-196952	19951117
	ES 2145936	T3	20000716	ES 1995-940031	19951117
	PT 793674	T	20001130	PT 1995-940031	19951117
	ZA 9509819	A	19960530	ZA 1995-9819	19951120
	TW 474924	B	20020201	TW 1995-84112388	19951120
	IL 116078	A1	19991231	IL 1995-116078	19951121
	US 5874585	A	19990223	US 1996-698575	19960815
	CA 2272548	AA	19980611	CA 1997-2272548	19971205
	WO 9824806	A2	19980611	WO 1997-US21636	19971205
	WO 9824806	A3	19981015		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9855894	A1	19980629	AU 1998-55894	19971205
	AU 734615	B2	20010621		
	EP 954526	A2	19991110	EP 1997-952232	19971205
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CN 1247542	A	20000315	CN 1997-180392	19971205
	TR 9901681	T2	20000321	TR 1999-9901681	19971205
	BR 9713684	A	20000328	BR 1997-13684	19971205
	JP 2001507679	T2	20010612	JP 1998-525656	19971205
	JP 3220169	B2	20011022		
	JP 2001192398	A2	20010717	JP 2000-197432	19971205
	TR 200103270	T2	20030321	TR 2001-200103270	19971205
	RU 2217436	C2	20031127	RU 1999-114606	19971205
	TW 593340	B	20040621	TW 1997-86118340	19971205
	US 6037325	A	20000314	US 1998-69823	19980430
	US 6001814	A	19991214	US 1998-90274	19980603
	NO 9902734	A	19990802	NO 1999-2734	19990604
	MX 9905240	A	20000531	MX 1999-5240	19990604
	US 2002119985	A1	20020829	US 2001-927832	20010810
	US 2002119998	A1	20020829	US 2001-991286	20011116
	US 6608175	B2	20030819		
	US 2003203851	A1	20031030	US 2002-125222	20020418
	US 6656911	B2	20031202		
PRAI	US 1994-345820	A2	19941121		
	US 1996-698575	A1	19960815		

L4 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

	US 1996-760916	A	19961206
	US 1996-761190	A	19961206
	US 1996-761313	A	19961206
	US 1996-762381	A	19961206
	US 1996-771317	A	19961206
	US 1997-984881	A	19971204
	US 1997-984884	A	19971204
	US 1997-985056	A	19971204
	US 1997-985201	A	19971204
	US 1997-985298	A	19971204
	JP 1998-525656	A3	19971205
	WO 1997-US21636	W	19971205

OS MARPAT 130:125406
GI

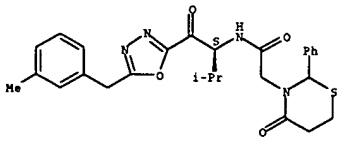
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to certain substituted oxadiazole, thiadiazole and triazole peptoids I [X, Y = O, N, S; at least one of X or Y = N; R1 = alkyl or alkenyl optionally substituted with halo or hydroxy; alkynyl, alkyl-CO2Me, dialkylamino, alkyldialkylamino; or cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, C5-12 aryl, C5-12 arylalkyl, C5-12 arylalkenyl optionally containing 1 or more heteroatoms N, S, O, and optionally substituted; R2, R3 = R'2, R'3 = independently H, alkyl, alkylthio, alkylthioalkyl, cycloalkyl, alkylcycloalkyl, Ph, phenylalkyl optionally substituted with guanidine, carboalkoxy, OH, haloalkyl, alkylthio, alkylguanidine, dialkylguanidine or amidine; R11, R12 and E together form a monocyclic or bicyclic ring comprising 5-10 atoms selected from C, N, S, and O; said ring containing 1 or more keto groups; and optionally substituted with halo, cyano, nitro, haloalkyl, amino, aminoalkyl, dialkylamino, alkyl, alkenyl, alkynyl, alkoxy, carboxyl, etc; or cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, C5-12 aryl, C5-12 arylalkyl, (C5-12 arylalkyl)OCONH, C5-12 arylalkenyl optionally containing 1 or more heteroatoms N, S, O, and optionally substituted], and pharmaceutically acceptable salts thereof, which are useful as inhibitors of human neutrophil elastase (HNE) for the treatment of HNE-mediated processes implicated in conditions such as adult respiratory distress syndrome, septic shock and multiple organ failure. A series of studies also have indicated the involvement HNE in myocardial ischemia-reperfusion injury, emphysema. HNE-mediated processes are implicated in other conditions such as arthritis, periodontal disease, glomerulonephritis, dermatitis, psoriasis, cystic fibrosis, chronic bronchitis, atherosclerosis, Alzheimer's disease, organ transplantation, corneal ulcers, and invasion behavior of malignant tumors. Thus, coupling of valine-derived oxadiazole II (R1 = CH2C6H4Me-3) (preparation given) with III (Cbz = PhCH2O2C), followed by oxidation of the secondary alc. to the corresponding ketone gave oxadiazole peptide derivative IV. IV inhibited human neutrophil elastase with Ki = 0.21 nM.

IT **208845-59-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of azole heterocyclic peptoids as serine protease inhibitors)
RN 208845-59-4 CAPLUS
CN 2H-1,3-Thiazine-3(4H)-acetamide, dihydro-N-[(1S)-2-methyl-1-[[5-[(3-methylphenyl)methyl]-1,3,4-oxadiazol-2-yl]carbonyl]propyl]-4-oxo-2-phenyl-

L4 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:604649 CAPLUS
DN 129:231017
TI Preparation of azole heterocyclic peptoids as serine protease inhibitors
IN Gyorkos, Albert; Spruce, Lyle W.
PA Cortech, Inc., USA
SO U.S., 62 pp., Cont.-in-part of U.S. 5,618,792.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 18

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5807829	A	19980915	US 1996-761190	19961206
	US 5618792	A	19970408	US 1994-345820	19941121
	CA 2205198	AA	19960530	CA 1995-2205198	19951117
	CA 2205198	C	20020604		
	CN 1170414	A	19980114	CN 1995-196952	19951117
	ES 2145936	T3	20000716	ES 1995-940031	19951117
	PT 793674	T	20001130	PT 1995-940031	19951117
	ZA 9509819	A	19960530	ZA 1995-9819	19951120
	TW 474924	B	20020201	TW 1995-84112388	19951120
	IL 116078	A1	19991231	IL 1995-116078	19951121
	US 5874585	A	19990223	US 1996-698575	19960815
	US 6159938	A	20001212	US 1997-859242	19970520
	US 6150334	A	20001121	US 1997-985201	19971204
	CA 2272548	AA	19980611	CA 1997-2272548	19971205
	WO 9824806	A2	19980611	WO 1997-US21636	19971205
	WO 9824806	A3	19981015		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9855894	A1	19980629	AU 1998-55894	19971205
	AU 734615	B2	20010621		
	EP 954526	A2	19991110	EP 1997-952232	19971205
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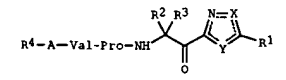
	CN 1247542	A	20000315	CN 1997-180392	19971205
	TR 9901681	T2	20000321	TR 1999-9901681	19971205
	BR 9713684	A	20000328	BR 1997-13684	19971205
	JP 2001507679	T2	20010612	JP 1998-525656	19971205
	JP 3220169	B2	20011022		
	JP 2001192398	A2	20010717	JP 2000-197432	19971205
	TR 200103270	T2	20030321	TR 2001-200103270	19971205
	RU 2217436	C2	20031127	RU 1999-114606	19971205
	TW 593340	B	20040621	TW 1997-86118340	19971205
	US 6037325	A	20000314	US 1998-69823	19980430
	US 6001813	A	19991214	US 1998-90046	19980603
	NO 9902734	A	19990802	NO 1999-2734	19990604
	MX 9905240	A	20000531	MX 1999-5240	19990604
PRAI	US 1994-345820	A2	19941121		
	US 1996-698575	A1	19960815		

L4 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

	US 1996-760916	A	19961206
	US 1996-761190	A2	19961206
	US 1996-761313	A	19961206
	US 1996-762381	A	19961206
	US 1996-771317	A	19961206
	US 1997-984881	A	19971204
	US 1997-984884	A	19971204
	US 1997-985056	A	19971204
	US 1997-985201	A	19971204
	US 1997-985298	A	19971204
	JP 1998-525656	A3	19971205
	WO 1997-US21636	W	19971205

OS MARPAT 129:231017
GI



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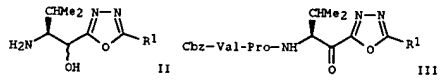


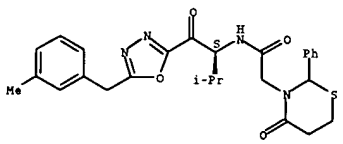
II III

AB The present invention relates to certain substituted oxadiazole, thiadiazole and triazole peptoids I [X, Y = O, N, S; at least one of X or Y = N; R1 = alkyl or alkenyl optionally substituted with halo or hydroxy; alkynyl, alkyl-CO2Me, dialkylamino, alkylidialkylamino; or cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, C5-12 aryl, C5-12 arylalkyl, C5-12 arylalkenyl optionally containing 1 or more heteroatoms N, S, O, and optionally substituted; R2, R3 = independently H, alkyl, alkylthio, alkylthioalkyl, cycloalkyl, alkylcycloalkyl, Ph, phenylalkyl optionally substituted with guanidine, carboalkoxy, OH, haloalkyl, alkylthio, alkylguanidine, dialkylguanidine or amidine; A = bond, CO, NHCO, SO2, O2C, CH2, amino acid residue; R4 = H, alkyl, alkenyl, cycloalkyl, aryl, arylalkyl, fused aryl-cycloalkyl optionally containing 1 or more heteroatoms N, O, S, and optionally substituted], and pharmaceutically acceptable salts thereof, which are useful as inhibitors of human neutrophil elastase (HNE) for the treatment of HNE-mediated processes implicated in conditions such as adult respiratory distress syndrome, septic shock and multiple organ failure. A series of studies also have indicated the involvement HNE in myocardial ischemia-reperfusion injury, emphysema. HNE-mediated processes are implicated in other conditions such as arthritis, periodontal disease, glomerulonephritis, dermatitis, psoriasis, cystic fibrosis, chronic bronchitis, atherosclerosis, Alzheimer's disease, organ transplantation, corneal ulcers, and invasion behavior of malignant tumors. Thus, coupling of valine-derived oxadiazole II (R1 = CH2C6H4Me-3) (preparation given) with Cbz-Val-Pro-OH (Cbz = PhCH2O2C), followed by oxidation of the secondary alc. to the corresponding ketone gave oxadiazole peptide derivative III. III inhibited human neutrophil elastase with Ki = 0.025 nM.

IT **208845-59-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of azole heterocyclic peptoids as serine protease inhibitors)

RN 208845-59-4 CAPLUS
CN 2H-1,3-Thiazine-3(4H)-acetamide, dihydro-N-[(1S)-2-methyl-1-[[5-[(3-methylphenyl)methyl]-1,3,4-oxadiazol-2-yl]carbonyl]propyl]-4-oxo-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:585365 CAPLUS
DN 129:216917
TI preparation of proline analog peptides as serine protease inhibitors
IN Gyorkos, Albert; Spruce, Lyle W.
PA Cortech, Inc., USA
SO U.S., 62 pp., Cont.-in-part of U. S. 5,618,792.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 18

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5801148	A	19980901	US 1996-771317	19961206
	US 5618792	A	19970408	US 1994-345820	19941121
	CA 2205198	AA	19960530	CA 1995-2205198	19951117
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	PT 793674	T	20001130	PT 1995-940031	19951117
	ZA 9509819	A	19960530	ZA 1995-9819	19951120
	TW 474924	B	20020201	TW 1995-84112388	19951120
	IL 116078	A1	19991231	IL 1995-116078	19951121
	US 5874585	A	19990223	US 1996-698575	19960815
	US 5998379	A	19991207	US 1997-985056	19971204
	CA 2272548	AA	19980611	CA 1997-2272548	19971205
	WO 9824806	A2	19980611	WO 1997-US21636	19971205
	WO 9824806	A3	19981015		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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	AU 9855894	A1	19980629	AU 1998-55894	19971205
	AU 734615	B2	20010621		
	EP 954526	A2	19991110	EP 1997-952232	19971205
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	CN 1247542	A	20000315	CN 1997-180392	19971205
	TR 9901681	T2	20000321	TR 1999-9901681	19971205
	JP 2001507679	T2	20010612	JP 1998-525656	19971205
	JP 3220169	B2	20011022		
	JP 2001192398	A2	20010717	JP 2000-197432	19971205
	TR 200103270	T2	20030321	TR 2001-200103270	19971205
	RU 2217436	C2	20031127	RU 1999-114606	19971205
	TW 593340	B	20040621	TW 1997-86118340	19971205
	US 6037325	A	20000314	US 1998-69823	19980430
	US 6100238	A	20000808	US 1998-89587	19980603
	NO 9902734	A	19990802	NO 1999-2734	19990604
	MX 9905240	A	20000531	MX 1999-5240	19990604
PRAI	US 1994-345820	A2	19941121		
	US 1996-698575	A1	19960815		
	US 1996-760916	A	19961206		
	US 1996-761190	A	19961206		

L4 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

	US 1996-761313	A	19961206		
	US 1996-762381	A	19961206		
	US 1996-771317	A2	19961206		
	US 1997-984881	A	19971204		
	US 1997-984884	A	19971204		
	US 1997-985056	A	19971204		
	US 1997-985201	A	19971204		
	US 1997-985298	A	19971204		
	JP 1998-525656	A3	19971205		
	WO 1997-US21636	W	19971205		

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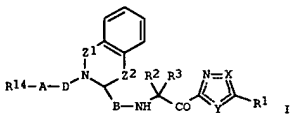

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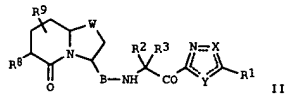


II

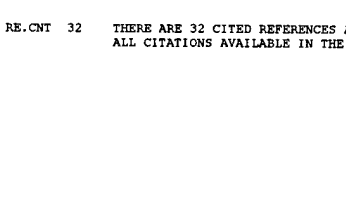
AB Proline analog peptides I and II [X, Y = O, N, S; R1 = alkyl, alkenyl, alkynyl, dialkylamino, etc.; R2, R3 = H, alkyl, alkylthio, alkylthioalkyl, etc.; B = SO2, CO; Z1, Z2 = direct bond or CH2; D = direct bond or certain amino acid residues; A = CO, NHCO, SO2, OCO, O2CNH, CH2; R14 = H, alkyl, alkenyl, cycloalkyl, aryl, arylalkyl, etc.; W = S, O; R8 = alkylamino, dialkylamino, amino; R9 = H, alkyl, halo] or their pharmaceutically acceptable salts were prepared as serine protease inhibitors. Thus, (benzyloxycarbonyl)-L-valyl-N-[1-[2-[5-(3-methylbenzyl)-1,3,4-oxadiazolyl]carbonyl]-2-(S)-methylprolyl]-L-prolinamide, prepared from 3-(S)-[(benzyloxycarbonyl)amino]-2-acetoxy-4-methylpentanenitrile, 3-methylphenylacetic hydrazide, and Cbz-Val-Pro-OH, showed inhibition activity Ki = 0.025 nM.

IT 208845-59-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of proline analog peptides as serine protease inhibitors)

RN 208845-59-4 CAPLUS

L4 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
CN 2H-1,3-Thiazine-3(4H)-acetamide, dihydro-N-[(1S)-2-methyl-1-[[5-[(3-methylphenyl)methyl]-1,3,4-oxadiazol-2-yl]carbonyl]propyl]-4-oxo-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:394350 CAPLUS
DN 129:68032
TI Preparation of oxadiazole peptide analogs as serine protease inhibitors
IN Gyorkos, Albert; Spruce, Lyle W.
PA Cortech, Inc., USA; Gyorkos, Albert; Spruce, Lyle W.
SO PCT Int. Appl., 187 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 18

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9824806	A2	19980611	WO 1997-US21636	19971205
	WO 9824806	A3	19981015		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5801148	A	19980901	US 1996-771317	19961206
	US 5807829	A	19980915	US 1996-761190	19961206
	US 5861380	A	19990119	US 1996-760916	19961206
	US 5869455	A	19990209	US 1996-761313	19961206
	US 5891852	A	19990406	US 1996-762381	19961206
	US 5998379	A	19991207	US 1997-985056	19971204
	US 6001811	A	19991214	US 1997-984884	19971204
	US 6015791	A	20000118	US 1997-984881	19971204
	US 6150334	A	20001121	US 1997-985201	19971204
	CA 2272548	AA	19980611	CA 1997-2272548	19971205
	AU 9855894	A1	19980629	AU 1998-55894	19971205
	AU 734615	B2	20010621		
	EP 954526	A2	19991110	EP 1997-952232	19971205
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 9713684	A	20000328	BR 1997-13684	19971205
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	US 1996-762381	A	19961206		
	US 1996-771317	A	19961206		
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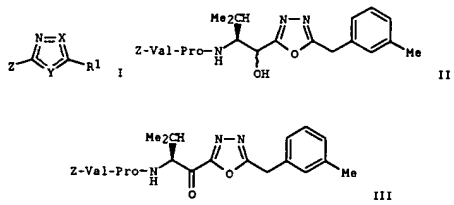
	US 1997-984884	A	19971204		
	US 1997-985056	A	19971204		
	US 1997-985201	A	19971204		
	US 1997-985298	A	19971204		
	US 1994-345820	A2	19941121		
	WO 1997-US21636	W	19971205		

OS MARPAT 129:68032
GI

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



I II

III

AB The present invention relates to certain substituted oxadiazole, thiadiazole and triazole peptide analogs I [X, Y = independently O, S, (un)substituted N; Z = serine protease binding moiety, preferably a human neutrophil elastase binding moiety; R1 = (un)substituted alkyl, alkenyl, alkynyl; OH, amino, alkylamino, dialkylamino, cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, cycloalkenyl, alkylcycloalkenyl, alkenylcycloalkenyl, C5-12 aryl, C5-12 arylalkyl, C5-12 arylalkenyl, fused C5-12 arylcycloalkyl, alkyl fused C5-12 arylcycloalkyl] which are useful as inhibitors of serine proteases. Thus, Swern oxidation of reduced pseudopeptide II (Z = PhCH2O2C), prepared in 8 steps from 3S-(benzyloxycarbonylamino)-2-acetoxy-4-methylpentanenitrile, 3-methylphenylacetic hydrazide, and Z-Val-Pro-OH, gave 74% desired oxadiazole III. III inhibited human neutrophil elastase with IC50 = 0.025 nM in an in vitro assay.

IT **208845-59-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

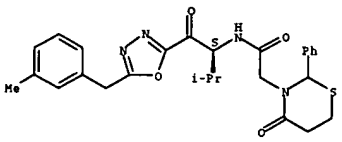
(preparation of oxadiazole peptide analogs as serine protease and human neutrophil elastase inhibitors)

RN 208845-59-4 CAPLUS

CN 2H-1,3-Thiazine-3(4H)-acetamide, dihydro-N-[(1S)-2-methyl-1-[[5-[(3-methylphenyl)methyl]-1,3,4-oxadiazol-2-yl]carbonyl]propyl]-4-oxo-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L4 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1969:409716 CAPLUS

DN 71:9716

TI Effect of structural variations on antioxidant capability. IV. Heterocycles with two heteroatoms

AU Fenech, Giovanna; Tommasini, Alessandro; Valenti, Giacomo

CS Ist. Chim. Farm. Tossicol., Univ. Messina, Messina, Italy

SO Atti della Societa Peloritana di Scienze Fisiche, Matematiche e Naturali (1967), 13(3-4), 157-71
CODEN: ASPSAJ; ISSN: 0037-8860

DT Journal

LA Italian

AB The antioxidant effect of title compds. toward vitamin C, at 60°, was in the following decreasing order: 2-phenyl-3-(R-substituted)-5-(R1-substituted)thiazolidin-4-one (I) (R = piperidin-3-yl, R1 = H), I (R = 2-methylpiperidin-6-yl, R1 = H), I (R = 3-methylpiperidin-6-yl, R1 = H), I (R = 4-methylpiperidin-2-yl, R1 = H), I (R = 3-methylpiperidin-2-yl, R1 = H), 2-phenyl-3-(R-substituted)-6-(R1-substituted)tetrahydro-1,3-thiazin-4-one (II) (R = piperidin-3-yl, R1 = H), I (R = piperidin-2-yl, R1 = H), I (R = piperidin-2-yl, R1 = Me), II (R = 2-methylpiperidin-6-yl, R1 = H), II (R = 3-methylpiperidin-6-yl, R1 = H), II (4-methylpiperidin-2-yl, R1 = H), II (R = piperidin-4-ylcarbamoyl, R1 = CO2H), II (R = piperidin-2-yl, R1 = H), II (R = piperidin-4-yl, R1 = H), I (R = NHCOC5H4N, R1 = CH2CO2H), I (R = NHCOC5H4N, R1 = H), I (R = NHCOC5H4N, R1 = Me), I (R = N:CHPh, R1 = CH2CO2H), I (R = N:CHPh, R1 = H) and I (R = N:CHPh, R1 = Me).

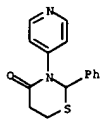
IT **10165-03-4**

RL: BIOL (Biological study)

(antioxidant activity of)

RN 10165-03-4 CAPLUS

CN 4H-1,3-Thiazin-4-one, tetrahydro-2-phenyl-3-(4-pyridyl)- (7CI, 8CI) (CA INDEX NAME)



L4 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1966:423765 CAPLUS

DN 65:23765

OREF 65:4439h,4440a-b

TI Relation of chemical structure to activity of heterocyclic sulfates

AU Fenech, Giovanna

SO Atti della Societa Peloritana di Scienze Fisiche, Matematiche e Naturali (1965), 11(1-2), 117-29
CODEN: ASPSAJ; ISSN: 0037-8860

DT Journal

LA Italian

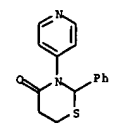
AB The antibacterial and pharmacol. effects of a series of thiazolidinones and metathiazanones were studied. Twenty-six compds. with and without ortho, meta, and para substitution of Cl or NO2 on the phenyl ring and a 2-, 3-, or 4-pyridyl ring or an isonicotinoylamino moiety on the N of the thiazole and metathiazanone rings were tested. Oral doses of 25-300 mg./kg. of various compds. were given rats kept under observation for characteristic central nervous system (CNS) effects. Antibacterial effects were followed by the agar diffusion technique using 6.3-mm. filter paper disks saturated with suspensions containing 20 γ/ml. of the compds. studied. Of the metathiazanones, 2-phenyl-3-(3-pyridyl)-1,3-thiazan-4-one and 2-phenyl- and 2-(2-chlorophenyl)-3-(4-pyridyl)-1,3-thiazanione had stimulating effects on the CNS at doses >50 mg./kg., characterized by tremors and tonic convulsions. A depressing action was noted at lower dose levels. Of the thiazolidinones studied 2-(3-nitrophenyl)-3-(3-pyridyl)-4-thiazolidinone had a weak CNS stimulating effect and 2-(2-chlorophenyl)- and 2-(3-nitrophenyl)-3-(isonicotinoylamino)-4-thiazolidinone had CNS depressing effects. Only 2-(2-nitrophenyl)-3-(2-pyridyl)-1,3-thiazan-4-one had a weak inhibiting effect on Staphylococcus aureus and Trichophyton mentagrophytes. The 6-membered Sheterocyclic ring, the unsubstituted phenyl ring, and the 4-pyridyl radical produced the greatest CNS effect.

IT **10165-03-4**, 4H-1,3-Thiazin-4-one, tetrahydro-2-phenyl-3-(4-pyridyl)- **10165-04-5**, 4H-1,3-Thiazin-4-one, 2-(o-chlorophenyl)tetrahydro-3-(4-pyridyl)-

(pharmacology of)

RN 10165-03-4 CAPLUS

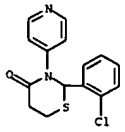
CN 4H-1,3-Thiazin-4-one, tetrahydro-2-phenyl-3-(4-pyridyl)- (7CI, 8CI) (CA INDEX NAME)



RN 10165-04-5 CAPLUS

CN 4H-1,3-Thiazin-4-one, 2-(o-chlorophenyl)tetrahydro-3-(4-pyridyl)- (7CI, 8CI) (CA INDEX NAME)

L4 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L4 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1962:66924 CAPLUS

DN 56:66924

OREF 56:12898e-g

TI Reactivity of the azomethine group. XI. Synthesis of 2-aryl-3-(3- and 4-pyridyl)-1,3-thiazan-4-ones

AU Fenech, Giovanna; Basile, Maria

CS Univ. Messina, Italy

SO Gazzetta Chimica Italiana (1961), 91, 163-72
CODEN: GCITA9; ISSN: 0016-5603

DT Journal

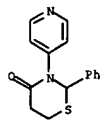
LA Unavailable

AB Reactions of Schiff bases from 3- and 4-aminopyridine with HS(CH2)2CO2H (I) were described. I and the Schiff base from 3-aminopyridine and BzH refluxed in dry C6H6 70 hrs., gave 2-phenyl-3-(3-pyridyl)-1,3-thiazan-4-one, m. 105-7°, together with some S(CH2CH2CO2H)2 and benzaldehyde thioacetal. The following 1,3-thiazan-4-ones were similarly obtained: 2-(2-chlorophenyl)-3-(3-pyridyl), m. 110-12°; 2-(3-nitrophenyl)-3-(3-pyridyl), m. 152-4°; 2-phenyl-3-(4-pyridyl), m. 190-1°; 2-(2-chlorophenyl)-3-(4-pyridyl), m. 201-3°. With p-O2NC6H4CHO, no cyclic compound was obtained. With m-O2NC6H4CHO and I in the presence of 4-aminopyridine a mixture of products was obtained, including a 1:1 compound of the acid and aldehyde.

IT **10165-03-4**, 4H-1,3-Thiazin-4-one, tetrahydro-2-phenyl-3-(4-pyridyl)- **10165-04-5**, 4H-1,3-Thiazin-4-one, 2-(o-chlorophenyl)tetrahydro-3-(4-pyridyl)-
(preparation of)

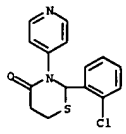
RN 10165-03-4 CAPLUS

CN 4H-1,3-Thiazin-4-one, tetrahydro-2-phenyl-3-(4-pyridyl)- (7CI, 8CI) (CA INDEX NAME)



RN 10165-04-5 CAPLUS

CN 4H-1,3-Thiazin-4-one, 2-(o-chlorophenyl)tetrahydro-3-(4-pyridyl)- (7CI, 8CI) (CA INDEX NAME)



L4 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

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L5 ANSWER 1 OF 2 CAOLD COPYRIGHT 2005 ACS on STN
AN CA65:4439h CAOLD
TI relation of chemical structure to activity of heterocyclic sulfates
AU Fenech, Giovanna
IT 10164-84-8 10164-85-9 10164-86-0 10164-87-1 10164-88-2 10164-89-3
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IT **10165-03-4** **10165-04-5**
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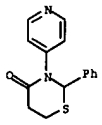
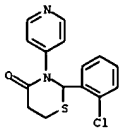


RN 10165-04-5 CAOLD
CN 4H-1,3-Thiazin-4-one, 2-(o-chlorophenyl)tetrahydro-3-(4-pyridyl)- (7CI, 8CI) (CA INDEX NAME)



L5 ANSWER 2 OF 2 CAOLD COPYRIGHT 2005 ACS on STN
AN CA56:12898g CAOLD
TI sulfinic acid amidines - (I) preparation of sulfinic acid amidines from amidine
derivs. and their cyclization to 1,2,4,6-thiatriazines
AU Goerdeler, Joachim; Wedekind, B.
IT **10165-03-4** **10165-04-5** 53245-14-0 97339-63-4
97379-78-7 97394-35-9 98028-89-8 98780-16-6 98780-17-7 99671-37-1
99801-23-7 99801-24-8 100146-98-3 100149-31-3 100153-92-2 100174-69-4
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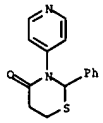
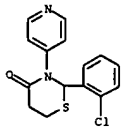
IT **10165-03-4** **10165-04-5**
RN 10165-03-4 CAOLD
CN 4H-1,3-Thiazin-4-one, tetrahydro-2-phenyl-3-(4-pyridyl)- (7CI, 8CI) (CA INDEX NAME)



RN 10165-04-5 CAOLD
CN 4H-1,3-Thiazin-4-one, 2-(o-chlorophenyl)tetrahydro-3-(4-pyridyl)- (7CI, 8CI) (CA INDEX NAME)



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L9          11 S L8 AND THIAZ?

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L9 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:657939 CAPLUS
TI Quinazolinones and benzothiazinones as novel sodium channel blockers
AU Victory, Sam F.; Sun, Qun; Limberis, Jim; Kyle, Donald J.
CS Discovery Research, Purdue Pharma, L.P, Cranbury, NJ, 08512, USA
SO Abstracts of Papers, 228th ACS National Meeting, Philadelphia, PA, United States, August 22-26, 2004 (2004), MEDI-075 Publisher: American Chemical Society, Washington, D. C.
CODEN: 69FTZ8
DT Conference; Meeting Abstract
LA English
AB V102862 is a potent state-dependent sodium channel blocker (Ki = 370 nM, rBIIa) that has been shown to be efficacious in the Chung model of neuropathic pain. Toward the discovery of a second-generation compound having an improved pharmaceutical profile, we embarked on a systematic structure-activity investigation aimed at replacing the semicarbazone moiety of V102862 with various heterocycles as a bioisosteric replacement. Our labs. have reported on several series of high affinity sodium channel blockers as part of this effort, including a series of compds. containing a **thiazolidinone** ring system as a replacement. Some of the most potent compds. in the **thiazolidinone** series possessed a hydrophobic aryl ether moiety, similar to V102862, and also a piperidinylethylamine moiety. To further explore the bioisosteric replacement of the semicarbazone moiety of V102862, several addnl. series of compds. were synthesized including those having a quinazolin-4(3H)-one or a 2,3-dihydro-benzothiazin-4-one core ring system. Within each of these new series, the optimized piperidinylethylamine group of the **thiazolidinone** series was held constant while the hydrophobic aryl ether moiety was varied, generating potent sodium channel blockers in each series. Details of the synthesis and SAR of analogs will be presented.

L9 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:657937 CAPLUS
TI Design and synthesis of novel potent aryl substituted benzimidazoles sodium channel blockers
AU Zhou, Xiaoming; Sun, Qun; Kyle, Donald J.; Ilyin, Victor; Limberis, Jim
CS Discovery Research, Purdue Pharma L.P, Cranbury, NJ, 08512, USA
SO Abstracts of Papers, 228th ACS National Meeting, Philadelphia, PA, United States, August 22-26, 2004 (2004), MEDI-073 Publisher: American Chemical Society, Washington, D. C.
CODEN: 69FTZ8
DT Conference; Meeting Abstract
LA English
AB V102862 is a state-dependent sodium channel blocker that is efficacious in animal models of neuropathic pain. However, an in vivo metabolism study in rats suggested that the semicarbazone moiety of V102862 could account for formation of toxic semicarbazide metabolites. In order to improve potency and pharmaceutical profile, a focused chemical library with various substituted **thiazolidinones** was prepared The lead compound 1 was identified with a Ki of 90 nM for state-dependent inhibition of Nav1.2 (rBIIa Na) channels co-expressed with beta 1 subunit in Xenopus oocytes. Further modification of the **thiazolidinone** compound 1 led to a series of novel potent aryl substituted benzimidazoles (e.g. 2) as sodium channel blockers.

L9 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:20339 CAPLUS
DN 140:77163
TI Preparation of **thiazolylpiperazines** for treating or preventing pain
IN Kyle, Donald J.; Sun, Qun
PA USA
SO U.S. Pat. Appl. Publ., 37 pp., which
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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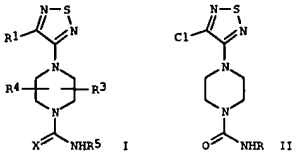
PRAI US 2002-360172P	P	20020301		
US 2002-411084P	P	20020917		

OS MARPAT 140:77163
GI



AB The title compds. [I; R1 = Me, halo; R3 = alkyl, alkenyl, alkynyl, etc.; R4 = H; R5 = alkyl, cycloalkyl, aryl, etc.; n = 0-2; X = O, S], useful for treating or preventing pain in a patient, were prepared E.g., a multi-step synthesis of three title compds. II [R = 4-tert-butylphenyl, 4-isopropylphenyl, and 4-trifluoromethylphenyl], was given. The compds. I were tested for binding to the human VR1 receptor. Typically, the compds. I have an IC50 of < 25 μM for inhibition of capsaicin-induced activation. Assays for testing binding of the compds. I to mGluR5 and to mGluR1 are described (no data). Pharmaceutical composition comprising the compound I is claimed.

L9 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:634845 CAPLUS
TI Parallel synthesis of a biased library of **thiazolidinones** as a novel sodium channel antagonists
AU Tafesse, Laykea; Sun, Qun; Limberis, James T.; Islam, Khondekar; Kyle, Donald J.
CS Purdue Pharma LP, Cranbury, NJ, 08512, USA
SO Abstracts of Papers, 226th ACS National Meeting, New York, NY, United States, September 7-11, 2003 (2003), MEDI-237 Publisher: American Chemical Society, Washington, D. C.
CODEN: 69EKY9
DT Conference; Meeting Abstract
LA English
AB A biased chemical library containing 91 differentially substituted **thiazolidinones** was prepared in an effort to improve the pharmacol. and to overcome certain development liabilities of a known anticonvulsant agent V102862. The collection was prepared in a single step multi-component condensation reaction that produced good yields and very high crude purity (75%-85%). Seven compds., identified within the library were shown to be more potent than V102862, our parent reference compound, in an electrophysiol.
assay measuring sodium channel antagonism. The most potent compound, 3-(2-piperidinylethyl)-2-(3-(3-trifluoromethylphenoxy)phenyl) **thiazolidinone**, has a Ki of 90 nM.

L9 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:625433 CAPLUS
DN 140:93967
TI Parallel synthesis of a biased library of **thiazolidinones** as novel sodium channel antagonists
AU **Sun, Qun**; Tafesse, Laykea; Limberis, James T.; Islam, Khondekar; **Kyle, Donald J.**
CS Purdue Pharma LP, Cranbury, NJ, 08512, USA
SO Combinatorial Chemistry and High Throughput Screening (2003), 6(5), 481-488
CODEN: CCHSFU; ISSN: 1386-2073
PB Bentham Science Publishers Ltd.
DT Journal
LA English
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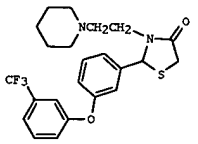
GI



I

AB A biased chemical library containing 91 differentially substituted **thiazolidinones**, e.g., I, was prepared in an effort to improve the pharmacol. of a known anticonvulsant agent V102862. The collection was prepared in a single-step multicomponent condensation reaction that produced the **thiazolidinones** in good yields and very high crude purity. Seven compds., identified within the library, were shown to be more potent than V102862, our parent reference compound, in an electrophysiol. assay measuring sodium channel antagonism. The most potent compound (I) has a Ki of 90 nM.
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
amelioration of both acute and chronic pain, of depression, as local anesthetics, as antiarrhythmics and for the treatment or prevention of diabetic neuropathy. The compds. of the invention are sodium channel blockers.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:76766 CAPLUS
DN 138:131144
TI Aryl-substituted **thiazolidinones** and therapeutic use thereof
IN **Sun, Qun; Kyle, Donald J.**
PA Euro-Celtique, S.A., Luxembourg
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003008398	A1	20030130	WO 2002-US22367	20020716
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003109521	A1	20030612	US 2002-195530	20020716
	EP 1417187	A1	20040512	EP 2002-763275	20020716
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	JP 2004538285	T2	20041224	JP 2003-513957	20020716
	US 2004176364	A1	20040909	US 2004-802765	20040318
PRAI	US 2001-305099P	P	20010716		
	US 2002-195530	A3	20020716		
	WO 2002-US22367	W	20020716		

OS MARPAT 138:131144
GI

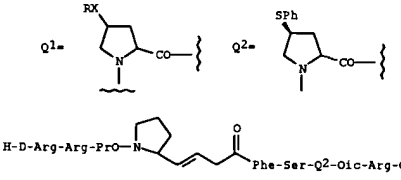
I

AB The invention discloses aryl-substituted **thiazolidinones** I [n = 1, 2; R1 = YN(R3)(R4) (Y = alkylene; R3, R4 = H, alkyl, aryl, or R3 and R4 together form alkylene chain having 4-5 C optionally interrupted by N or O), pyridylalkyl, optionally substituted piperidin-4-yl; R2 = optionally substituted phenoxyphenyl, optionally substituted phenylthiophenyl, optionally substituted benzyloxyphenyl, etc.], or a pharmaceutically acceptable salt or solvate thereof. The invention also discloses the use of I for the treatment of neuronal damage following global and focal ischemia, for the treatment or prevention of neurodegenerative conditions, e.g. amyotrophic lateral sclerosis, and for the treatment, prevention or

L9 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:563622 CAPLUS
DN 125:301602
TI Preparation of aminoalkenoate pseudopeptide derivatives as bradykinin antagonists
IN **Kyle, Donald J.**; Mavunkel, Babu J.
PA Scios Nova Inc., USA
SO U.S., 19 pp., Cont.-in-part of U. S. Ser. No. 957,879.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5552383	A	19960903	US 1993-118550	19930909
	US 5521158	A	19960528	US 1992-957879	19921008
	US 5686565	A	19971111	US 1994-281904	19940728
	CA 2171446	AA	19950316	CA 1994-2171446	19940909
	CA 2171446	C	20041123		
	WO 9507294	A1	19950316	WO 1994-US10128	19940909
	W: CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 716661	A1	19960619	EP 1994-929158	19940909
	EP 716661	B1	20000405		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 11500100	T2	19990106	JP 1994-508795	19940909
	AT 191486	E	20000415	AT 1994-929158	19940909
	ES 2148347	T3	20001016	ES 1994-929158	19940909
	US 5817756	A	19981006	US 1995-401595	19950309
	US 5610142	A	19970311	US 1995-416524	19950403
PRAI	US 1992-957879	A2	19921008		
	US 1993-118550	A2	19930909		
	US 1993-118558	A	19930909		
	US 1993-118981	A	19930909		
	US 1993-119341	A	19930909		
	US 1994-281904	A	19940728		
	US 1994-281906	A	19940728		
	US 1994-281907	A	19940728		
	US 1994-281908	A	19940728		
	US 1994-119341	A	19940909		
	WO 1994-US10128	W	19940909		
	US 1994-353426	B2	19941209		

OS MARPAT 125:301602
GI



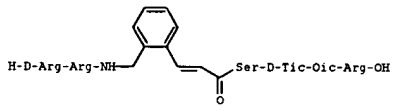
I

L9 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
AB A-B-C-D-E-F-G-H-I-J-Cn [A = H, D- and L- Arg, Gln, Asn, Lys, Sar, N-ε-Ac-Lys, NG-p-tosyl-Arg, NG-NO2-Arg, Lys-Lys, Ac-Arg, citrulline; B = bond, D- and L- Arg, Gln, Asn, Lys, Sar, Ne-Ac-Lys, NG-p-tosyl-Arg, NG-NO2-Arg, Ac-Arg, citrulline; C = bond, Pro, 4Hyp, Oic, dehydroPro, Tic, Aoc, L-azetidine-2-carboxylate, Eac, Gly, Thz, Aib; D = 2-pyrrolidinyl, Pro, 4Hyp, Oic, dehydroPro, Tic, Aoc, L-azetidine-2-carboxylate, Eac, Gly, Thz, Aib; E = X(CH2)mZ1(CH2)nZ2(CH2)oCHYCO; X = bond, NH; Z1, Z2 = bond, C3-8 carbocycle residue, (cyclic) alkenylene; Y = H, CH2OH, alkyl, PhCH2, thiophenylmethyl, furylmethyl; m, n, o = 0-12; m+n+o ≤12; F = bond, aromatic amino acid; G = bond, Ser, Thr, Gly, Val, Ala, Cys, Tyr; H = D-aromatic amino acid, D-Hype; I = Oic, Aoc, Thz, Tic, L-indoline-2-carboxylic acid, Aib, Leu, Ile, Val, Thi, octahydro-1H-isoindole-1-carboxylate, pipecolinic acid, Pro, 4Hyp, azetidine-2-carboxylate, Phe, homoPhe, Hype; J = Arg, Orn, Asn, Gln, Lys; Hype = Q1; R = (substituted) alkyl, cycloalkyl, aryl, aralkyl, etc.; X = O, S, SO, SO2; Cn = OH, amide, alkoxy, D- or L- amino acid residue; Aib = 2-aminoisobutyrate; Aoc = (S,S,S)-2-azabicyclo[3.3.0]octane-3-carboxylate; Eac = ε-aminocaproate; dehydroPro = 3,4-dehydroproline; 4Hyp = 4-hydroxyproline; Thi = β-2-thienylalanine; Thz = thiazolidine-4-carboxylate; Tic = tetrahydroisoquinoline-3-carboxylate; Oic = (2S, 3aS,7aS)-octahydro-1H-indole-2-carboxylate], were prepared Thus, title compound (I) antagonized bradykinin with Ki = 15 μM.

L9 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:494750 CAPLUS
DN 125:196389
TI Bradykinin antagonist pseudopeptide derivatives of aminoalkenoic acids
IN Kyle, Donald J.
PA Scios Nova Inc., USA
SO U.S., 26 pp., Cont.-in-part of U.S. 5,444,046.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5541286	A	19960730	US 1994-281907	19940728
	US 5521158	A	19960528	US 1992-957879	19921008
	US 5444048	A	19950822	US 1993-118981	19930909
	CA 2171446	AA	19950316	CA 1994-2171446	19940909
	CA 2171446	C	20041123		
	WO 9507294	A1	19950316	WO 1994-US10128	19940909
	W: CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 716661	A1	19960619	EP 1994-929158	19940909
	EP 716661	B1	20000405		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 11500100	T2	19990106	JP 1994-508795	19940909
	AT 191486	E	20000415	AT 1994-929158	19940909
	ES 2148347	T3	20001016	ES 1994-929158	19940909
	US 5817756	A	19981006	US 1995-401595	19950309
	US 5610142	A	19970311	US 1995-416524	19950403
PRAI	US 1992-957879	A2	19921008		
	US 1993-118981	A2	19930909		
	US 1993-118550	A	19930909		
	US 1993-118558	A	19930909		
	US 1993-119341	A	19930909		
	US 1994-281904	A	19940728		
	US 1994-281906	A	19940728		
	US 1994-281907	A	19940728		
	US 1994-281908	A	19940728		
	US 1994-119341	A	19940909		
	WO 1994-US10128	W	19940909		
	US 1994-353426	B2	19941209		

OS MARPAT 125:196389
GI



I

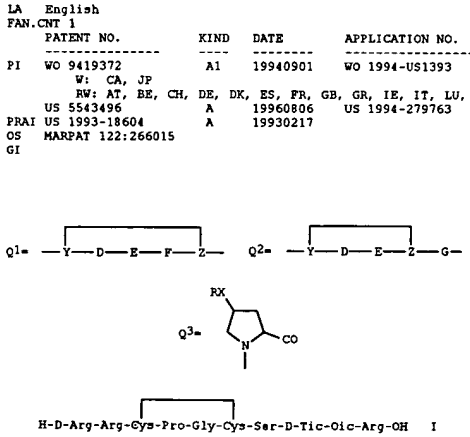
AB Pseudopeptide compds. A-B-C-D-E-F-G-Cn wherein: A is H or is selected from L- and D-isomers of, e.g., Arg, Gln, Asn, Lys; B is a bond or is selected

L9 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
from L- and D-isomers of Arg, Gln, Asn, Lys; C is a C2 to C18 olefinic aminoalkenoyl NH(CH2)mZ1(CH2)nZ2(CH2)oCO wherein Z1 and Z2 are independently selected from the group consisting of a bond, C3-8 carbocycle, C2-18 monoolefin or C4-18 polyolefin contg. 1-5 double bonds which may optionally be incorporated into a cyclic system; m, n, and o are independently 0-12, with the proviso that their total does not exceed 16; D is a bond or is selected from Ser, Thr, Gly, Val, Ala, Cys, and Tyr; E is selected from the group consisting of a D-arom. amino acid and a D-Hype (hydroxyproline ether/thioether); F is selected from, e.g., Oic, Aoc, Thz, Tic [Oic is (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid; Aoc is (S,S,S)-2-azabicyclo[3.3.0]octane-3-carboxylic acid; Thz is thiazolidine-4-carboxylic acid; Tic is tetrahydroisoquinoline-3-carboxylic acid]; G is selected from Arg, Orn, Asn, Gln, and Lys; Cn is OH or a C-terminal extension selected from, e.g., amide, alkoxy, based on a modified bradykinin sequence are potent bradykinin receptor antagonists. Amino acids at at positions 2 through 5 are replaced by olefinic aminoalkenoyl groups to reduce the peptide nature of the compds. The analogs produced are useful in treating conditions and diseases of a mammal and human in which an excess of bradykinin or related kinins are produced or injected such as by insect bites. Thus, e.g., pseudopeptide I was prepd. by solid-phase methodol., incorporating aminoalkenoyl spacer N-Boc-3-[2-(aminomethyl)phenyl]-2-propenoic acid (also prepd.); I exhibited binding to human bradykinin B2 receptor with K = 27 nM, and bradykinin antagonist activity with pA2 = 120 ± 8.

L9 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:502939 CAPLUS
DN 122:266015
TI Preparation of cyclic peptides as bradykinin antagonists.
IN Kyle, Donald James; Chakravarty, Sarvajit
PA Scios Nova Inc., USA
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9419372	A1	19940901	WO 1994-US1393	19940208
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5543496	A	19960806	US 1994-279763	19940725
PRAI	US 1993-18604	A	19930217		

OS MARPAT 122:266015
GI



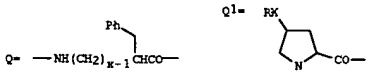
I

AB H-A1-A2-A3-A4-A5-A6-R1 [A1, A2 = D- or L-Arg, -Gln, -Asn, -Lys(Ac), -Lys, Lys-Lys, Sar, etc.; A3 = Q1, Q2; Y, Z = amino acid residues forming covalent bonds through their side chains; D, E = Pro, 4Hyp, Tic, Ala, Gly, Oic, Thz, Aib, dehydroprolyl, etc.; F = Phe, Thi, Trp, Tyr, Leu, Ile, Tic, Oic, hPhe, Nal, Val, phenylglycyl, etc.; G = bond, Ser, Thr, Gly, Val, Ala, Cys, Tyr; A4 = D-Phe, D-Tic, D-Pro, Q3; R = H, (substituted) alkyl, aryl, aralkyl, alkenyl, cycloalkyl, etc.; X = O, S, SO, SO2; A5 = Oic, Aoc, Tic, Pro, Aib, Leu, Ile, Val, Thi, Phe, hPhe, Q3, etc.; A6 = Arg, Orn, Asn, Gln, Lys; R1 = OH, amide, alkoxy, D- or L-amino acid or peptide residue; 4Hyp = 4-hydroxyprolyl; hPhe = homophenylalanyl, Thi = β-2-thienylalanyl, Tic = tetrahydroisoquinolin-3-carboxylic acid residue; Oic = (2S, 3aS, 7aS)-octahydro-1H-indole-2-carboxylic acid residue; Thz = thiazolidine-4-carboxylic acid residue; Aib = 2-aminoisobutyric acid residue], were prepared Thus, title compound (I; prepared using FMOC chemical) antagonized bradykinin in guinea pig intestinal strips with pA2 = 6.6.

L9 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:339374 CAPLUS
DN 123:9926
TI Preparation of novel pseudopeptide bradykinin receptor antagonists
IN **Kyle, Donald James**; Mavunkel, Babu Joseph
PA Scios Nova Inc., USA
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9408607	A1	19940428	WO 1993-US9130	19930927
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5521158	A	19960528	US 1992-957879	19921008
	US 5610142	A	19970311	US 1995-416524	19950403
PRAI	US 1992-957879	A	19921008		
	US 1993-118558	B1	19930909		

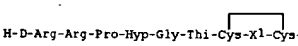
OS MARPAT 123:9926
GI



AB The substitution of at least one of the amino acids in positions 2 to 5 of the bradykinin peptide with a fatty acid amide converts bradykinin agonists into bradykinin antagonists. The invention further includes the intermediate compds. and addnl. modifications at other positions within the modified bradykinin antagonists which increase enzyme resistance, antagonist potency and/or specificity of the new bradykinin antagonists. This bradykinin-type peptides are represented by the formula R1-A-B-C-D-E-E-F-G-H-I-J-Cn [R1 = hydrogen; A, B = D- or L-Arg, -Gln, -Asn, -Lys, or -Lys(Ac), Arg(Tos), Arg(NO2), Lys-Lys, Ac-D-Arg, L-citrulline; C, D = direct bond, Pro, dehydro-Pro, 4-hydroxy-Pro (4Hyp), tetrahydroisoquinoline-3-carboxylic acid (Tic), (S,S,S)-2-azabicyclo[3.3.0]octane-3-carboxylic acid (Aoc), L-azetidine-2-carboxylic acid, ε-aminocaproic acid (Eac), Gly, **thiazolidine**-4-carboxylic acid (Thz), (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid (Oic), 2-aminoisobutyric acid (Aib), NH(CH2)xCO, Q (wherein x = 2-18); E = direct bond, Gly, Ala, Thr, Ser, NH(CH2)xCO, Q (wherein x = 2-18); F = direct bond, Phe, β-2-thienylalanine (Thi), Leu, Ile, Tic, Oic, homo-Phe, phenyl-Gly, β-cyclohexylalanine, Val, β-naphthyl-Ala (Nal), Val, NH(CH2)xCO, Q (wherein x = 2-18); G = Ser, Thr, 4Hyp, Gly, Val, Ala; H = D-Tic, D-Phe, trans-D-Q1 (wherein R = alkyl, alkenyl, aryl, aralkyl etc.; X = S, O); I = Phe, Tic, homo-Pro, cis- or trans-L-Q1, etc.; J = Arg, Lys, Orn, Asn, Gln, Lys(Ac), Orn(Ac); Cn = OH, amide, alkoxy, D- or L-amino acid residue, peptide residue containing D- or L-amino acids]. The analogs produced are useful for treating human or mammalian conditions and diseases in which an excess of bradykinin or

L9 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
related kinins is produced or injected as by insect bites, particularly for treating local pain and inflammation from burns, wounds, cuts, rashes, other trauma and pathol. conditions (no data). Thus, D-Arg-Arg-Pro-4Hyp-Gly-Thi-Ser-D-Phe-Oic-Arg-OH was prepd. by the solid phase method using a peptide synthesizer (model 9,600; Milligen Biosearch) Boc-Arg(Tos)-PAM resin and N-Boc-protected amino acids including Boc-Oic-OH, Boc-Thi-OH, and Boc-4Hyp(Bzl)-OH.

L9 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1991:144010 CAPLUS
DN 114:144010
TI Design and conformational analysis of several highly potent bradykinin receptor antagonists
AU **Kyle, Donald J.**; Martin, Jennifer A.; Farmer, Stephen G.; Burch, Ronald M.
CS Nova Pharm. Corp., Baltimore, MD, 21224, USA
SO Journal of Medicinal Chemistry (1991), 34(3), 1230-3
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
GI



IV

AB Drawing on the reported spectroscopic data for bradykinin in solution and, in particular, the possible significance of β-turn structures at the C-terminus of bradykinin receptor-active compds., five peptides H-D-Arg-Arg-Pro-Hyp-Gly-Thi-Ser-D-Tic-X-Arg-OH [Thi = L-4-**thiazolidinecarboxylic** acid, Tic = 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid; X = L-Tic (I), D-Tic (II), (1R,4S,5R)-2-azabicyclo[3.3.3]octane-4-carboxylic acid (III)], and IV [X1 = D-Tic-Phe-Arg, R = OH; X1 = D-Phe-Phe, R = Arg-OH) were prepared to challenge the hypothesis and probe the geometric and electronic requirements of the bradykinin receptor. Peptides I, II, and III were expected to stabilize the β-turn via conformationally constrained dihedral angles ψ, .vphi., and χ for the amino acids at positions i and i+1 of the β-turn. Subsequent conformational anal. using empirical energy calcns. suggested that only peptides I and III should adopt the desired turn, a result verified by the inactivity of peptide II in the binding assay. Both peptides I and III were highly potent bradykinin receptor antagonists. The β-turn was anticipated to exist in peptides IV due to the disulfide bond cyclization bridging the amino acids at the C-terminus. Energy calcns. performed on these peptides suggested a diminished likelihood of a C-terminal type II' β-turn due to the presence of cis amide bonds and like peptide II, were found to have no activity in the bradykinin receptor binding assay. These peptides support the hypothesis that peptide bradykinin receptor antagonists must adopt a β-turn geometry at their C-terminus in order to have a high affinity for the receptor as suggested by previous NMR expts. in nonpolar solvent systems.